



Treatment Resistant Depression

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What is Treatment Resistant Depression (TRD)?

- A subset of Major Depressive Disorder (MDD)
- MDD that is unresponsive to traditional and first-line therapeutic options
- Illness is termed TRD after 2 adequate antidepressant pharmacotherapy trials have failed
- Patients with major depression are often resistant to antidepressant monotherapy

Maudsley Guidelines for TRD

- The Maudsley Staging Method (MSM) was developed in 2009
- It is a point-based method that categorizes resistance as mild, moderate, or severe
- It assists with guiding treatment
- 3-6 = Mild
- 7-10 = Moderate
- 11-15 = Severe

Parameter/Dimension	Parameter Specification	Score
Duration	Acute (≤ 12 mo)	1
	Subacute (13-24 mo)	2
	Chronic (> 24 mo)	3
Symptom severity at baseline	Subsyndromal	1
	Syndromal	
	▪ Mid	2
	▪ Moderate	3
	▪ Severe without psychosis	4
▪ Severe with psychosis	5	
Treatment Failures Antidepressants	Level 1: 1-2 medications	1
	Level 2: 3-4 medications	2
	Level 3: 5-6 medications	3
	Level 4: 7-10 medications	4
	Level 5: > 10 medications	5
Augmentation	Not used	0
	Used	1
Electroconvulsive therapy	Not used	0
	Used	1
Total		15

What pharmacological strategies can be used in TRD?

- A high score in the Maudsley Staging Method (MSM) calls for doctors to choose the next treatment with a high impact and large effect
- There are 2 pharmacological strategies that can be used to treat TRD
 1. Augmentation = add a 2nd medication to current treatment
 2. Switch = change medication

When to Switch or Augment?

SWITCH to Another Antidepressant	AUGMENT With Another Medication
It is the first antidepressant trial	≥ 2 failed antidepressant trials
Poorly tolerated side effects to initial antidepressant	Initial antidepressant well tolerated
<25% improvement in symptoms on initial antidepressant (no response)	>25% improvement in symptoms on initial antidepressant (partial response)
Less severe symptoms, functional impairment	More severe symptoms, functional impairment
Patient preference to switch	Patient preference for adding medication
	To target specific residual symptoms or AEs of the initial antidepressant

- According to CANMAT 2023 MDD Guidelines:
 - If there is a < 20% improvement in symptoms by week #4, optimize therapeutic dose.
 - Then consider Augmentation or Switch pharmacological strategies

What to consider when deciding on Adjunctive or Switching therapies?

Patient Specific

Degree of Benefit vs Risk of current treatment

of unresponsive treatment trials

Patient's preference

Resources

- Hazari, Hiral, et al. “The Clinical Utility of Different Quantitative Methods for Measuring Treatment Resistance in Major Depression.” *Journal of Affective Disorders*, vol. 150, no. 2, Sept. 2013, pp. 231–236, <https://doi.org/10.1016/j.jad.2013.03.030>.
- “Transforming MDD Care: A Comprehensive Look at Adjunctive Treatment Options.” *Deceraclinical.com*, 2025, deceracclinical.com/education/activities/psychiatry/mdd-adjunctive-care-dl/128456/info.
- Voineskos, Daphne, et al. “Management of Treatment-Resistant Depression: Challenges and Strategies.” *Neuropsychiatric Disease and Treatment*, vol. Volume 16, no. 16, 21 Jan. 2020, pp. 221–234, [pmc.ncbi.nlm.nih.gov/articles/PMC6982454/](https://pubmed.ncbi.nlm.nih.gov/articles/PMC6982454/).